

## **REMARKS**

The Specification has been amended as required. In ¶0050, the derivative description is amended from "nucleophilic" to "electrophilic reactive" to correct an error; this is not new matter, at least because one skilled in the art knows that the stated sulfonyl chloride is a reactive electrophilic, not nucleophilic, derivative.

Claims 1-24 are pending and are rejected. Claims 11-14 and 22 are amended; claims 11-13 and 22 to correct the requested grammatical error noted in claim 11, which also appears in claims 12 and 22, and claim 14 as requested to provide antecedent basis. The amendments are fully supported in the application as filed, and contain no new matter.

Applicant thanks the Examiner and SPE Weber for the courtesy of a personal interview on September 13, 2006. As required, Applicant states that the substance of the interview was the pending rejections, specifically, how the applied Nikiforov patents neither anticipate nor render obvious Applicant's claims for the reasons provided below. As requested, Applicant asserts that the applied Nikiforov patents do not inherently disclose, teach, suggest, or motivate Applicant's claimed fluorescence quench-based assay, at least because of the Nikiforov '141 disclosure at col. 11 lines 10-22 that "...a variety of detection schemes may be employed which detect the rate of rotation of a molecule or the translation or lateral diffusion of a molecule that relates to the size of the molecule". These examples do not disclose quenching, nor would quenching inherently result. For example, Nikiforov's embodiment using a multivalent metal ion uses the ion to complex a large binding component to the fluorescent probe, and locates the metal ion within the much larger binding component. This is not in proximity to the fluorophore to result in quenching, as Applicant claims.

## **DOUBLE PATENTING**

Claims 1-14, 22, 23, and 24 are provisionally rejected under U.S.C. §101 over claims 1-11, 28, 37, 63 and 64 of co-pending Application No. 10/865,893.

The rejection is not applicable as it relates to claims 1-11 in the co-pending application because claims 1-11 were withdrawn in Applicant's Election. With respect to claims 28, 27, 63, and 64 in the co-pending Application, upon notice of allowable claims, Applicant will make amendments if necessary to overcome the rejection.

Claims 15-21 are provisionally rejected on nonstatutory obviousness-type double patenting over claims 29, 32, 34, 35, 37, and 38 of co-pending Application No. 10/865,893. Upon notice of allowable claims, Applicant will file a terminal disclaimer if necessary to overcome the rejection.

## **CLAIM OBJECTIONS**

Claim 11 is objected to because of informalities. Applicant has amended claim 11 to overcome the objection. Claims 12-13 also contains the noted informality, and are likewise amended.

## **CLAIM REJECTIONS UNDER 35 USC §112**

Claims 1-14, 19, and 22-24 are rejected under 35 USC §112 ¶1 as not enabled. Applicant respectfully disagrees.

Applicant's disclosed method is applicable for many enzymes, supported at least at p. 6 ¶16 "More specifically, the method of the present invention involves assaying the activity of an enzyme of choice by ...", and at p. 5 ¶18 "The method of this invention is particularly applicable in the assay of kinase and phosphatase activity...." One skilled in the art knows that all such enzymes function in the same general way in that they modify a substrate to produce a product, and that, without undue experimentation, particular substrate requirements for a specific enzyme class are readily available or determinable. Thus, Applicant asserts that his disclosure is enabling for enzymes other than kinases and phosphatases, and should not be limited to specific embodiments.

Claims 19-21 are rejected under 35 USC §112 ¶2 as indefinite. Claim 14, from which claims 19-21 depend, has been amended to provide the required antecedent basis.

Applicant thus believe the rejections under 35 U.S.C. §112, ¶1 and ¶2 are overcome and respectfully request their withdrawal.

#### **CLAIM REJECTIONS UNDER 35 USC §102**

Claims 1, 2, 4-6, 8, 9, and 11-13 are rejected under 35 USC §102(e) as anticipated by Nikiforov U.S. Patent No. 6,699,655 as evidenced by Cox. Applicant respectfully disagrees.

Nikiforov's '655 composition does not anticipate Applicant's claims 1, 2, 4-6, 8 and 9 at least because each of these claims requires a spatial arrangement of the components in its composition which Nikiforov '655 lacks.

Nikiforov's '655 composition results from fluorescence polarization. Applicant's claimed composition is formed in a fluorescence quench assay. It will not and cannot be formed by fluorescence polarization, because the conditions required to form Applicant's composition are absent in fluorescence polarization.

Nikiforov's '655 composition does not require the spatial arrangement and compound identity as in Applicants' composition. Nikiforov '655 discloses only a large "binding component" of between 5 kD and 1000 kD comprising a large polyionic compound or, alternatively, containing a multivalent metal ion. Its composition is largely irrelevant as long as it contains sufficient mass and is charged. A multivalent metal ion used alone in Nikiforov '655 would not be sufficient to affect the fluorophore in a fluorescence polarization assay, and would require conjugating the ion to a much larger "binding component" so that a resulting change in the fluorophore rotation could be measured.

In contrast, Applicant's claims 1, 2, 4-6, 8 and 9 require the following arrangement:

- the substrate must contain the fluorophore.
- the substrate must also contain the target group.
- the target group must have the paramagnetic metal ion is bound to it, forming a complex of the target group and the paramagnetic metal ion,
- this complex must be in proximity to the fluorophore, so that quenching can result when the complex forms.

Because Nikiforov's '655 composition lacks these elements, Applicant asserts that Nikiforov '655 does not anticipate these claims and respectfully request the rejection be withdrawn.

Claims 1, 2, 4-6, 8, 9, and 11-13 are rejected under 35 USC §102(e) as anticipated by Nikiforov U.S. Patent No. 6,472,141 as evidenced by Cox. Applicant respectfully disagrees.

Applicant incorporates his previous analysis, because Nikiforov '141 also exclusively discloses fluorescence polarization as the assay method. Further, Nikiforov '141 reiterates the nonspecific nature of the interaction between the "binding component" and the fluorescent probe:

The polyions used in accordance with the present invention are generally capable of interacting with the other components of the reaction mixture in a non-specific charge dependent manner. As a non-specific interaction, it will be appreciated that the polyions used in accordance with the present invention do not require the presence of a specific recognition site in the product (or substrate). (column 9, line 15).

Thus, Applicant's method relies on a spatial relationship between the quenching ion and the fluorophore. Nikiforov '141 relies on a non-specific interaction based solely on charge difference to impart mass to the probe to decrease the rotation of the probe and increasing the polarization of the fluorescence.

For at least these reasons, Applicant asserts that the rejections under 35 §102 are overcome and respectfully requests their withdrawal.

#### **CLAIM REJECTIONS UNDER 35 USC §103**

Claims 1-24 are rejected under 35 USC §103(a) as obvious over Nikiforov U.S. Patent No. 6,472,141 as evidenced by Cox. Applicant respectfully disagrees.

As previously explained, Nikiforov '141 discloses a fluorescence polarization assay. In contrast, Applicant's claims 1-24 recite fluorescence quenching. "A composition formed in a fluorescence quench-based homogenous assay..." (claims 1-13) and "A method for assaying the activity of an enzyme comprising [steps omitted]... causing the specific quenching of the fluorescence from the fluorophore..." (claims 14-24). Fluorescence polarization is not the same as, and does not teach, suggest, or motivate fluorescence quenching. The techniques differ as explained above, and also differ in other properties known to one skilled in the art, at least including how each is initiated. As only one example, fluorescence polarization requires a source of plane-polarized light to initiate the process; fluorescence quenching does not require this.

One skilled in the art would not be taught, suggested, or motivated by Nikiforov '141 to change its fluorescence polarization assay to a fluorescence quench-based assay. Nikiforov '141 provides no suggestion to do so. Further, even if there was such a teaching, suggestion, or motivation, which Applicant disputes, it would not result in Applicant's claimed invention, at least because the Nikiforov '141 composition does not require the spatial arrangement of components as Applicant previously described.

Thus, because the rejection fails at least due to of lack of motivation to combine and because of reasonable expectation of success, Applicant believes he has overcome the §103 rejection and respectfully requests its withdrawal.

**CONCLUSION**

Applicant believes the application is now in complete condition for allowance, and that no fee is due. If fees or surcharges are deemed due, Applicant authorizes charging them to Deposit Account No. 23-3000.

The Examiner is invited to contact Applicant's undersigned representative with any questions or issues.

Respectfully submitted,  
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